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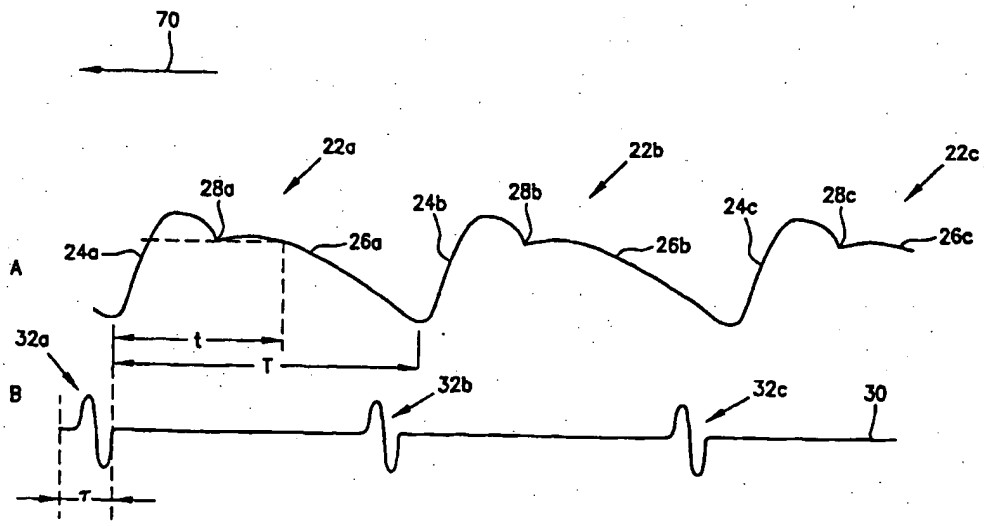

(57) Abstract

A noninvasive method of monitoring the intracranial pressure (ICP) of a patient. At least one waveform representative of a pulsation of an anatomical feature of the patient's head is obtained, preferably by integrating ultrasound reflection traces in a time gate corresponding to reflections from the feature. The preferred anatomical feature is the third cerebral ventricle. A quantitative measure of ICP is inferred from two or more diagnostic features, such as diagnostic times, associated with the waveform. Alternatively, a qualitative measure of ICP is obtained from the shape of the respiratory wave imposed on the train of waveforms by the patient's breathing.

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NONINVASIVE MONITORING OF INTRACRANIAL PRESSURE

FIELD AND BACKGROUND OF THE INVENTION

The present invention relates to noninvasive medical diagnostics and, more particularly, to a noninvasive method of monitoring intracranial pressure.

Abnormal intracranial pressure (ICP) is diagnostic of brain and skull pathologies, including head injuries, abnormal growths in the brain, and hemorrhages. The normal ICP is between about 10 mm Hg and about 12 mm Hg. An ICP greater than about 20 mm Hg causes headaches. An ICP greater than about 40 mm Hg causes coma.

Presently known methods of monitoring ICP are predominantly invasive.

In lumbar puncture, a needle is inserted at the base of the spinal column, to monitor the pressure of the fluid in the spinal column. This pressure may not reflect accurately the ICP, because there may be a blockage between the patient's head and the base of the patient's spinal column.

A second invasive method of monitoring ICP is to make a burr hole 10 mm in diameter in the patient's skull and to introduce a catheter to one of the lateral ventricles via the hole. The pressure of the cerebrospinal fluid (CSF) in the ventricle is measured directly by a transducer via the catheter. This procedure may cause a hemorrhage that blocks the penetrated ventricle. In addition, if CSF enters the catheter, the accuracy of the pressure reading is impaired.

In a related invasive method, the catheter is held in place by a threaded fitting that is screwed into the patient's skull. A saline solution is introduced to the catheter and the pressure of the saline solution is measured using an appropriate transducer. If insufficient care is taken to preserve antiseptic conditions, this procedure may lead to infection of the patient's brain.

Furthermore, the threaded fitting may penetrate the patient's brain, causing damage to the patient's brain.

In both of the latter two invasive methods, the catheter must be removed after five days. Therefore, these methods can not be used for long term (several months) monitoring of ICP of patients in comas.

In a fourth invasive method, a fiber optic device, with a sensor at the tip of a fiber optic cable, is inserted in the patient's cerebral tissue, in the patient's subdural space, or in the patient's intraventricular epidural space. If a blood clot forms on the sensor, or if the fiber optic cable bends too sharply or breaks, the device may give a spuriously high pressure reading.

In short, the prior art invasive methods of measuring ICP are unreliable, may lead to infection, and can not be used for more than five consecutive days.

There are additional reasons why it would be advantageous to have a non-invasive method of monitoring ICP.

The standard quantitative measure of the severity of coma is the Glasgow Coma Scale. See Mark S. Greenberg (ed.), *Handbook of Neurosurgery*, 4th edition (1988), vol. 2 p. 553. The score value of the scale ranges from 15 for a normal individual to 3 for a patient in deep coma. The prior art protocol is to start ICP monitoring if the score is 8 or less. It would be useful to monitor ICP of patients with scores higher than 8.

It also would be useful to monitor the ICP of healthy individuals under severe environmental stress, for example, astronauts, divers and submariners.

Yost et al., in US Patent No. 5,617,873, purport to describe an indirect, noninvasive method of monitoring ICP. Two changes in CSF volume are induced, and the associated changes in ICP are measured. The absolute value of ICP is inferred from these measurements. Although

the methods they teach for measuring the changes in ICP in fact are noninvasive, their methods of *inducing* changes in CSF volume are necessarily invasive, despite their claims to the contrary.

Transcranial Doppler monitoring is a noninvasive technique that provides only qualitative indications of variations in ICP, not the quantitative measurements provided by the prior art invasive methods.

Michaeli, in US Patent No. 5,840,018, which is incorporated by reference for all purposes as if fully set forth herein, teaches a noninvasive method for diagnosis of migraines, based on ultrasound measurements of the diameters of cranial blood vessels. Ultrasound reflection traces are integrated within a preselected gate to provide samples of an Echo Pulsogram (EPG) signal. The timing of the gate is selected to correspond to the depth within the cranium of the target blood vessel. The time lag between start systole, as indicated by an Electrocardiograph (ECG) signal, and the start of contraction of the target blood vessel, as compared to the normal time lag of 211±6 milliseconds, is diagnostic of migraines.

SUMMARY OF THE INVENTION

According to the present invention there is provided a method for measuring intracranial pressure in a head of a patient, the head including a forehead and a bridge of a nose, including the steps of: (a) measuring, entirely from outside the head of the patient, at least one waveform representative of a pulsation of an anatomical feature in the head of the patient; (b) identifying a plurality of diagnostic features associated with the at least one waveform; and (c) inferring the intracranial pressure from the plurality of diagnostic features.

The shapes of anatomical features of a patient's skull, such as the cerebral ventricles, change in synchrony with the patient's heartbeat. The present invention is based on an empirical relationship between these shape pulsations and ICP. According to the present invention, a waveform, or a series of waveforms, representative of the pulsation of the shape of one of these anatomical features, is measured noninvasively, and the empirical relationship is used to infer

ICP. The preferred anatomical feature is the third ventricle. The preferred modality for measuring the waveform is ultrasound. The preferred waveform is obtained by integrating ultrasound reflection traces within a predetermined gate corresponding to a reflection from the anatomical feature.

According to a first embodiment of the present invention, a ratio of diagnostic times that characterize the waveform is determined. An empirical quadratic relationship between this ratio and ICP as measured by a prior art invasive method is used to infer ICP quantitatively.

According to a second embodiment of the present invention, several successive waveforms are received, over the course of at least one respiratory cycle. The shape of the corresponding respiratory wave, as reflected in the successive waveforms, is related qualitatively to the ICP.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention is herein described, by way of example only, with reference to the accompanying drawings, wherein:

FIG. 1A is a sketch of EPG waveforms over the course of several cardiac cycles;

FIG. 1B is a sketch of an ECG trace synchronous with the waveforms of FIG 1A;

FIG. 2 shows ρ as a function of t/T;

FIGS. 3A and 3B are sketches of waveform trains modulated by a patient's breathing.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention is of a noninvasive method of quantitative and qualitative monitoring of ICP.

The principles and operation of noninvasive monitoring of ICP according to the present invention may be better understood with reference to the drawings and the accompanying description.

As used herein, a waveform is said to be representative of a pulsation of an anatomic feature if the shape of the waveform, as a function of time, is isomorphic with the shape of the anatomical feature, as a function of time, up to a sign. For example, the geometric dimensions of a patient's third ventricle increase and decrease in synchrony with the change in the patient's blood pressure over the course of the patient's cardiac cycle. A waveform whose amplitude increases as a corresponding dimension of the third ventricle increases, and whose amplitude decreases as that dimension of the third ventricle decreases, is said to be representative of the pulsation of the third ventricle over the course of the cardiac cycle. This isomorphic representation is up to a sign, so a waveform whose amplitude decreases as a corresponding dimension of the third ventricle increases, and whose amplitude increases as a corresponding dimension of the third ventricle decreases, also is said to be representative of the pulsation of the third ventricle over the course of the cardiac cycle.

Although the scope of the present invention includes the measurement of waveforms representative of any anatomical feature of a patient's head, including, for example, the frontal cornum, the temporal cornum and the occipital cornum of the first and second ventricles, as well as the fourth ventricle, the preferred anatomical feature is the third ventricle. Again, although the scope of the present invention includes any noninvasive modality for measuring waveforms representative of pulsations of the target anatomical feature, the preferred modality is ultrasound. An ultrasound transducer is placed in contact with the patient's forehead. Pulses of ultrasound energy are introduced to the patient's head, in the saggital direction, using the transducer. These pulses are partly reflected from anatomical features, including the target anatomical feature, that lie in their propagation paths. The reflections propagate back to the transducer, where they are converted into reflection traces. The desired waveforms are obtained by integrating each of the traces within a predefined gate, as taught in US Patent No. 5,840,018. Each resulting integration value is a sample of an EPG waveform.

Referring now to the drawings, Figure 1A shows two EPG waveforms **22a** and **22b** and a part of a third waveform **22c** thus obtained, as a function of time. Each waveform **22** includes a monotonically rising portion **24** and a falling portion **26**, with falling portion **26** including a venous output notch **28**. For reference, Figure 1B shows an ECG trace **30**, synchronized with EPG waveforms **22**, that includes several ECG pulses **32**. The start of each waveform **22** is coincident with the end of the corresponding ECG pulse **32**. The direction of movement is indicated by an arrow **70**. The start of each EPG waveform **22** is delayed relative to the start of the corresponding ECG pulse **32** by a delay τ.

It has been determined empirically that the best location for the ultrasound transducer on the forehead of the patient is from 2.5 centimeters to 6 centimeters above the bridge of the patient's nose.

The features of waveforms **22** that are diagnostic of ICP are two diagnostic times T and t, shown in Figure 1A with reference to waveform **22a**. Diagnostic time T is the duration of waveform **22**, i.e., the duration of one cardiac cycle. Diagnostic time t is the length of time from the start of waveform **22** until the time, subsequent to the time of venous output notch **28**, at which the amplitude of failing portion **26** returns to the amplitude of waveform **22** at the time of venous output notch **28**. Because time t is shorter than the full duration of one waveform **22**, time t is referred to herein as a "subduration".

By calibrating with invasive measures of ICP, it has been determined that the following equation describes ICP in terms of the ratio t/T with a 96% correlation:

$$ICP = \rho(t/T) - B$$

The constant B is 9 mm H_2O. For t/T less than about 0.3, ρ also is a constant, 373 mm H_2O. For t/T greater than about 0.5, ρ itself varies quadratically with t/T, as shown in Figure 2. Note that the units of the ordinate in Figure 2 are mm H_2O.

As the patient breathes, the train of waveforms **22** shown in part by Figure 1A may be modulated by that breathing. If the ICP is less than 15 mm Hg, the overall shape of the train of waveforms **22** is flat, as in Figure 1A, over many cardiac cycles. It is known from invasive studies that if the ICP is greater than about 20 mm Hg, the train of waveforms **22** is modulated by a respiratory wave (Greenberg, *op. cit.*, pp. 710-711). If the ICP is in the range of 20 to 40 mm Hg, the respiratory wave is in the form of a β-wave **40**, as shown in Figure 3A. β-wave **40** includes cycles **42** of roughly equal periodicity that tend to have sharp peaks **44** and smooth troughs **46**. Diagnostic features **42, 44** and **46** of β-wave **40** define the shape of β-wave **40** as roughly sinusoidal. If the ICP is in the range of 40 to 60 mm Hg, the respiratory wave is in the form of a plateau wave **50**, as shown in Figure 3B. The shape of plateau wave **50** is defined by a series of cycles **52**, with each cycle **52** starting with a sharp rise **54** to a sharp peak **56**, declining to a plateau **58**, and then declining further to a baseline **60**. Monitoring successive waveforms **22** over several respiratory cycles to observe the shape of the respiratory wave provides a qualitative indication of ICP .

While the invention has been described with respect to a limited number of embodiments, it will be appreciated that many variations, modifications and other applications of the invention may be made.

WHAT IS CLAIMED IS:

1. A method for measuring intracranial pressure in a head of a patient, the head including a forehead and a bridge of a nose, comprising the steps of:

(a) measuring, entirely from outside the head of the patient, at least one waveform representative of a pulsation of a ventricle in the head of the patient;

(b) identifying a plurality of diagnostic features associated with said at least one waveform; and

(c) inferring the intracranial pressure from said plurality of diagnostic features.

2. The method of claim 1, wherein said ventricle is a third ventricle.

3. The method of claim 1, wherein said measuring of said waveform is effected by steps including repeatedly receiving ultrasound echoes from said anatomical feature, said echoes defining said waveform.

4. The method of claim 3, wherein said receiving of said ultrasound echoes is effected by steps including:

(i) placing an ultrasound transducer in contact with the head of the patient;

(ii) repeatedly introducing pulses of ultrasound energy into the head of the patient, using said transducer; and

(iii) for each of said pulses, receiving a reflection trace of said pulse.

5. The method of claim 4, wherein said waveform is obtained from said reflection traces by integrating each of said reflection traces within a predetermined gate, said integration of said each reflection trace providing a sample of said waveform.

6. The method of claim 4, wherein said receiving of said reflection traces is effected using said transducer.

7. The method of claim 6, wherein said ultrasound transducer is placed in contact with the forehead of the patient, between about 2.5 centimeters and about 6 centimeters above the bridge of the nose.

8. The method of claim 1, wherein said plurality of diagnostic features includes a plurality of diagnostic times.

9. The method of claim 8, wherein said plurality of diagnostic times includes a duration and a subduration.

10. The method of claim 9, wherein the intracranial pressure is inferred from a ratio of said subduration to said duration.

11. The method of claim 10, wherein the intracranial pressure is inferred from a linear function of said ratio.

12. The method of claim 1, wherein said measuring of said at least one waveform is effected for a sufficiently long time to include at least one respiratory wave.

13. The method of claim 12, wherein said plurality of diagnostic features defines a shape of said at least one respiratory wave.

14. A method for measuring intracranial pressure in a head of a patient, the head including a forehead and a bridge of a nose, comprising the steps of:

(a) measuring, entirely from outside the head of the patient, at least one waveform representative of a pulsation of an anatomical feature in the head of the patient by:

(i) placing an ultrasound transducer in contact with the forehead of the patient, between about 2.5 centimeters and about 6 centimeters above the bridge of the nose,

(ii) repeatedly introducing pulses of ultrasound energy into the head of the patient, using said transducer, and

(iii) for each of said pulses, receiving a reflection trace of said pulse, using said transducer, said reflection traces defining said waveform;

(b) identifying a plurality of diagnostic features associated with said at least one waveform; and

(c) inferring the intracranial pressure from said plurality of diagnostic features.

15. A method for measuring intracranial pressure in a head of a patient, comprising the steps of:

(a) measuring, entirely from outside the head of the patient, at least one waveform representative of a pulsation of an anatomical feature in the head of the patient;

(b) identifying a duration and a subduration associated with said at least one waveform; and

(c) inferring the intracranial pressure from said duration and said subduration.

16. A method for measuring intracranial pressure in a head of a patient, comprising the steps of:

(a) measuring, entirely from outside the head of the patient, for a sufficiently long time to include at least one respiratory wave, at least one EPG waveform representative of a pulsation of an anatomical feature in the head of the patient;

(b) identifying a plurality of diagnostic features, associated with said at least one waveform, that define a shape of said respiratory wave; and

(c) inferring the intracranial pressure from said plurality of diagnostic features.

17. A method for measuring intracranial pressure in a head of a patient, comprising the steps of:

(a) measuring, entirely from outside the head of the patient, at least one EPG waveform representative of a pulsation of an anatomical feature in the head of the patient;

(b) identifying a plurality of diagnostic features associated with said at least one waveform; and

(c) inferring the intracranial pressure from said plurality of diagnostic features.

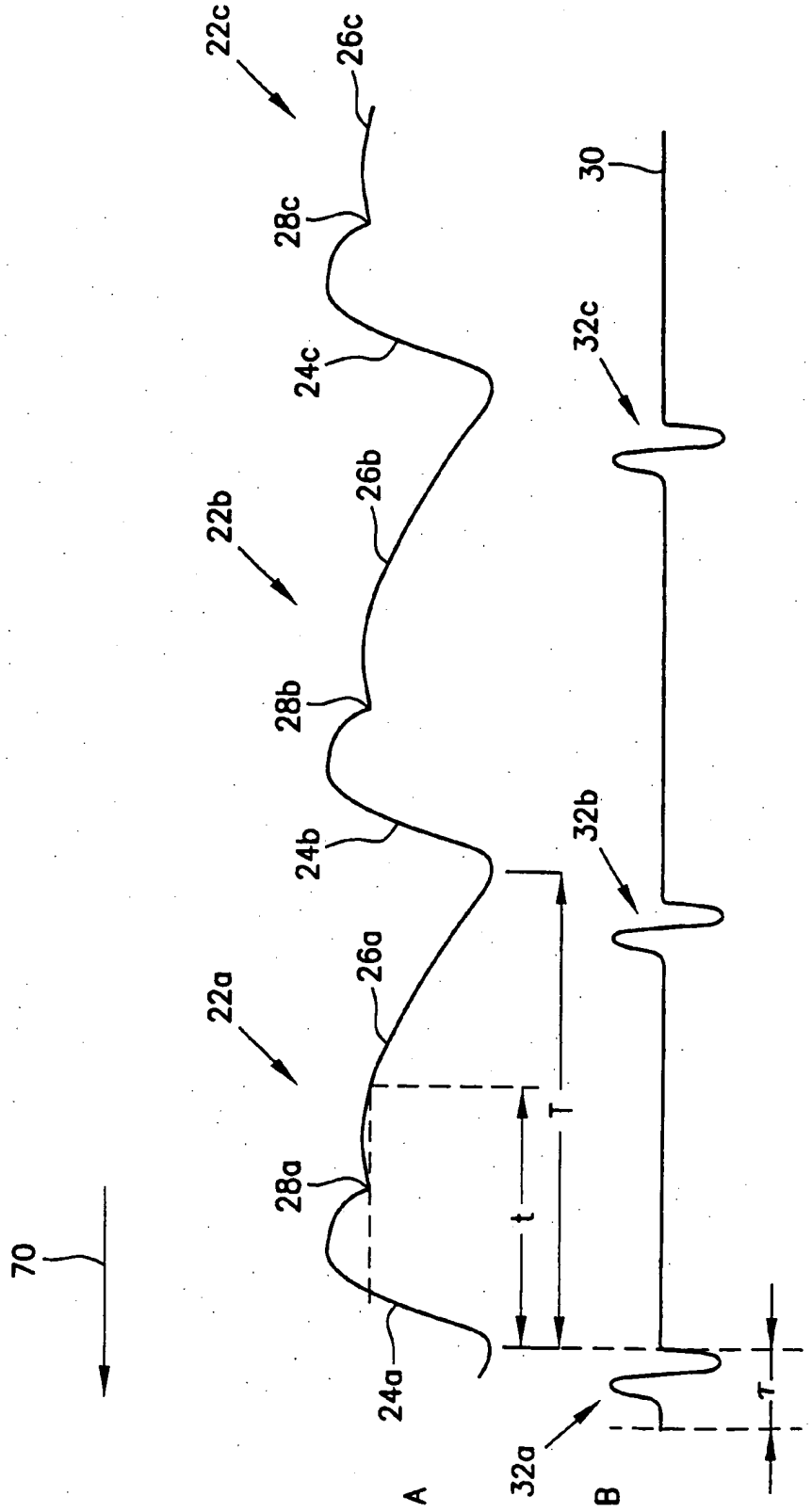
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Fig. 1

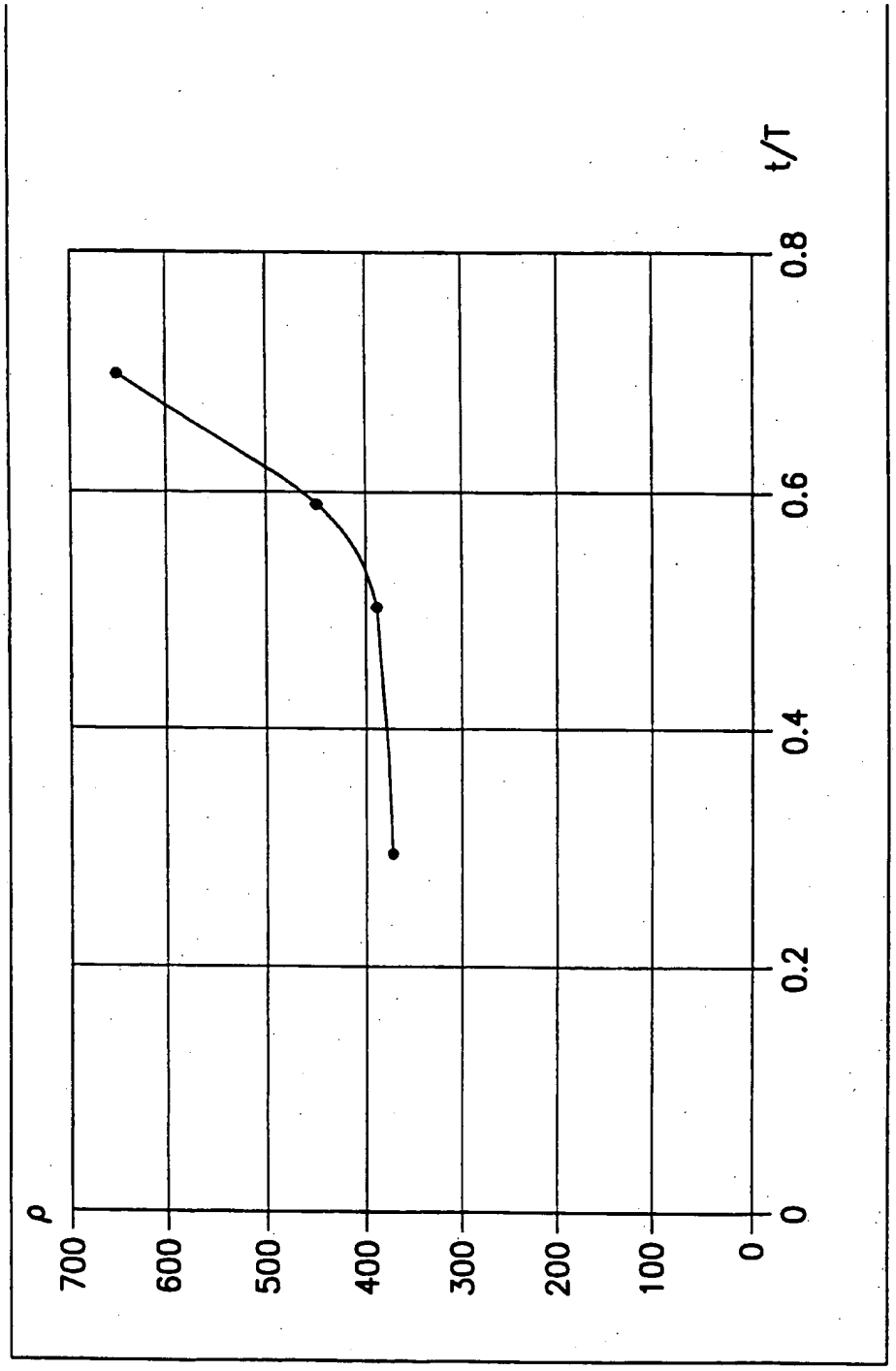

Fig. 2

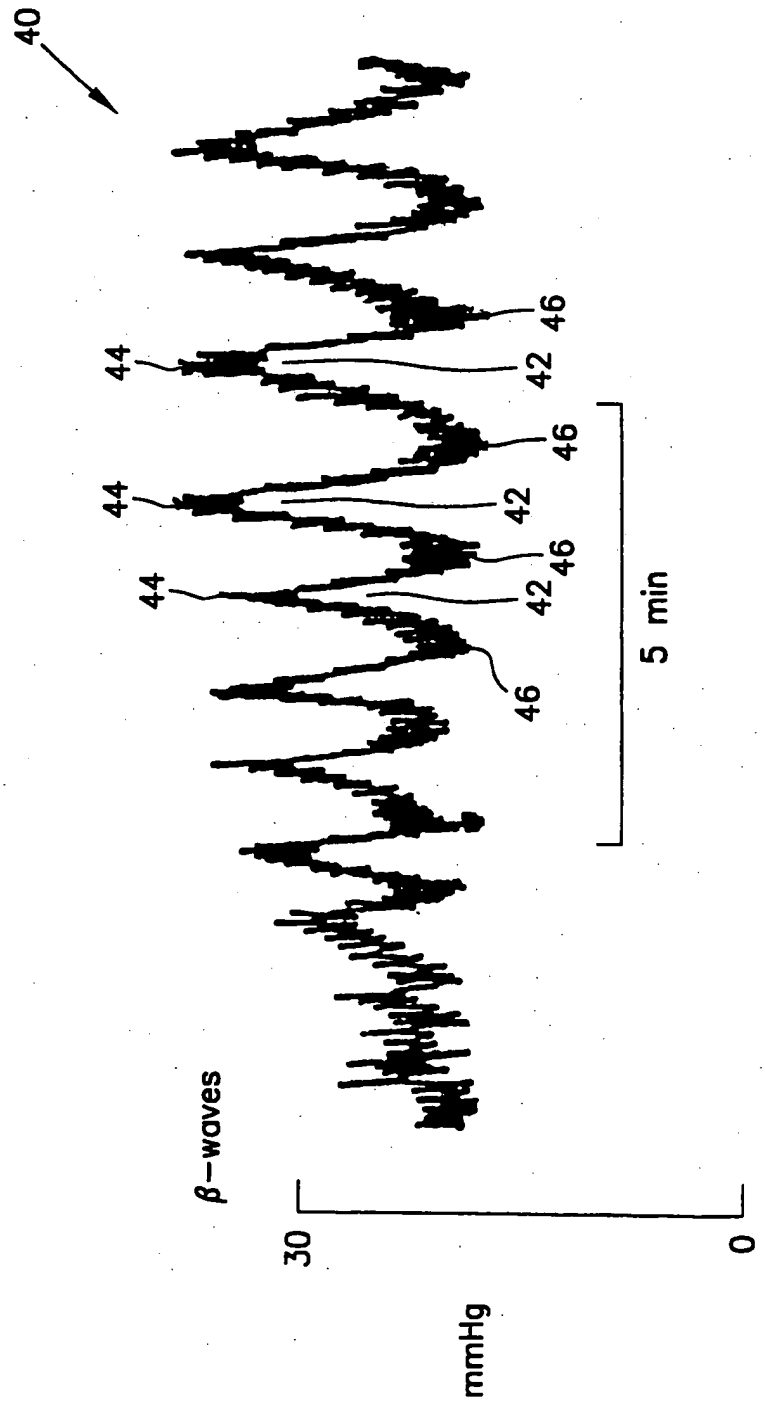

Fig. 3A

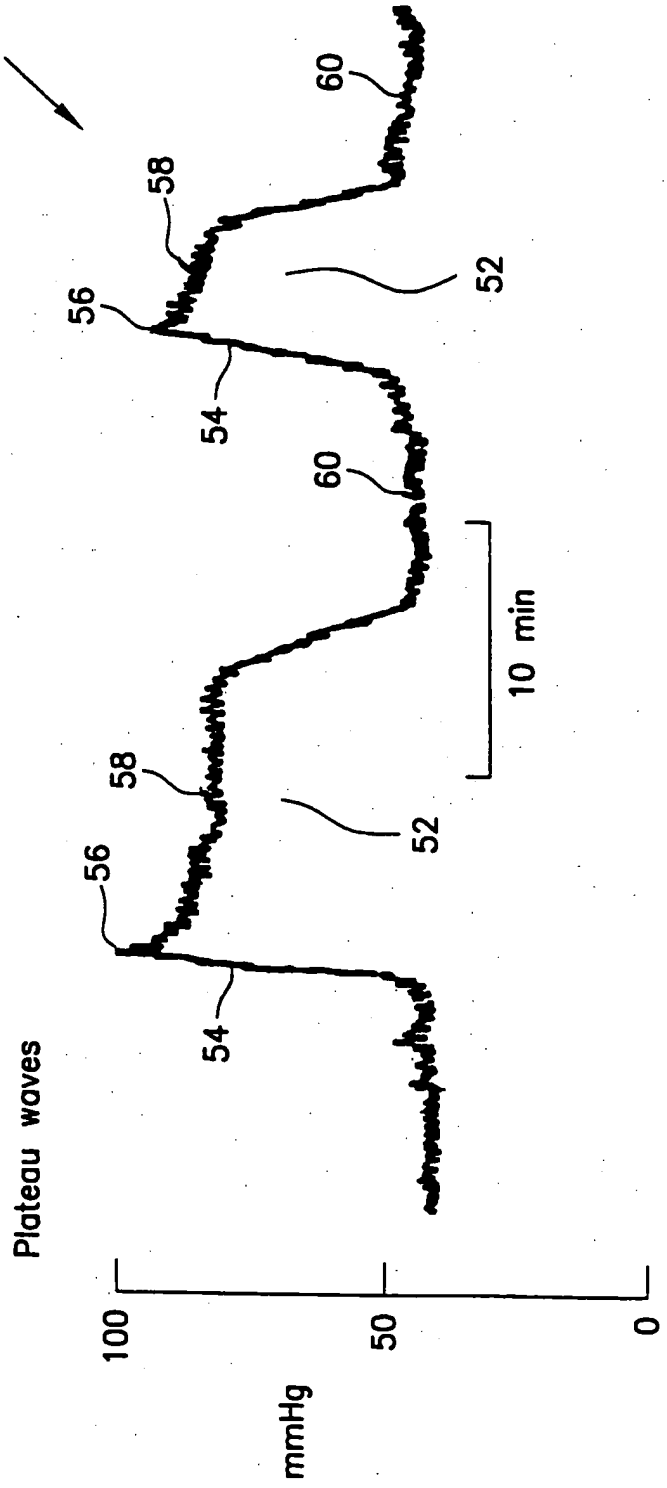

Fig. 3B